PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:
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FILE No. 27867
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PCT

NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY REPORT ON PATAENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Rule 71.1)

Date of mailing *(day/month/year)* 22 AUG 2005	
Applicant's or agent's file reference 27867	**IMPORTANT NOTIFICATION**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/IL04/00305	01 April 2004 (01.04.2004)	04 April 2003 (04.04.2003)

Applicant

BIOVIEW LTD.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary report on patentability and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary report on patentability. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the *PCT Applicant's Guide*.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed invention is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the IPEA/ US Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Sheela J. Huff Telephone No. 571-272-1600

Form PCT/IPEA/416 (January 2004)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 27867	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. PCT/IL04/00305	International filing date *(day/month/year)* 01 April 2004 (01.04.2004)	Priority date *(day/month/year)* 04 April 2003 (04.04.2003)
International Patent Classification (IPC) or national classification and IPC IPC(7): G01N 33/53 and US Cl.: 435/7.1. 7.21, 7.7,7.9, 40.5, 40.51, 40.52		
Applicant BIOVIEW LTD.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 6 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *(sent to the applicant and to the International Bureau)* a total of 11 sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s))
      _____ , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items:
   - ☒ Box No. I Basis of the report
   - ☐ Box No. II Priority
   - ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - ☐ Box No. IV Lack of unity of invention
   - ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - ☐ Box No. VI Certain documents cited
   - ☐ Box No. VII Certain defects in the international application
   - ☐ Box No. VIII Certain observations on the international application

Date of submission of the demand	Date of completion of this report
21 April 2005 (21.04.2005)	04 August 2005 (04.08.2005)
Name and mailing address of the IPEA/ US Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Sheela J. Huff J. Roberts for Telephone No. 571-272-1600

Form PCT/IPEA/409 (cover sheet)(January 2004)

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
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Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language _____, which is the language of a translation furnished for the purposes of:

☐ international search (under Rules 12.3 and 23.1(b))

☐ publication of the international application (under Rule 12.4)

☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☐ the international application as originally filed/furnished

☒ the description:
pages 1-34 as originally filed/furnished
pages* NONE received by this Authority on _____
pages* NONE received by this Authority on _____

☒ the claims:
pages NONE as originally filed/furnished
pages* NONE as amended (together with any statement) under Article 19
pages* 35-45 received by this Authority on 21 April 2005 (21.04.2005)
pages* NONE received by this Authority on _____

☒ the drawings:
pages 1-4 as originally filed/furnished
pages* NONE received by this Authority on _____
pages* NONE received by this Authority on _____

☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. ☒ The amendments have resulted in the cancellation of:

☒ the description, pages none
☒ the claims, Nos none
☒ the drawings, sheets/figs none
☒ the sequence listing (*specify*): none
☒ any table(s) related to the sequence listing (*specify*): none

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____
☐ the claims, Nos _____
☐ the drawings, sheets/figs _____
☐ the sequence listing (*specify*): _____
☐ any table(s) related to the sequence listing (*specify*): _____

** If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 72-75

because:

☐ the said international application, or the said claim Nos. _____ relate to the following subject matter which does not require an international preliminary examination *(specify)*:

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _____ are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 72-75

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See Supplemental Box for further details.

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims 6,9,14-18,24,26-27,29-30,32-71	YES
	Claims 1-5,7-8,10-13,19-23,25,28,31	NO
Inventive Step (IS)	Claims 6,9,14-15,17-18,24,26-27,29,30,32-71	YES
	Claims 1-5, 7-8,10-13,16,19-23,25,28,31	NO
Industrial Applicability (IA)	Claims 1-71	YES
	Claims NONE	NO

2. Citations and Explanations (Rule 70.7)
Please See Continuation Sheet

Supplemental Box

In case **the space in any of the preceding boxes is not sufficient.**

Continuation of:

V. 2. Citations and Explanations:

Claims 1-5, 7, 10-13, 19-23, 25, 28 and 31 lack novelty under PCT Article 33(2) as being anticipated by McCORMICK et al.
This reference describes the assessment of HER2 using two different stains (immunohistochemical and fluorescence in situ hybridization. The analysis was done in formalin-fixed, paraffin-embedded breast tumors.

Applicant argues that in the instant invention the same sample is stained twice and in the reference two different sections are used. Applicant is arguing limitations not found in the claims.

Claims 1-5, 8, 19-23 and 25 lack novelty under PCT Article 33(2) as being anticipated by VAN AGTHOVAN et al.
This reference describes the assessment of malignant breast tissues using dual staining immunohistochemistry.

Applicant argues that the reference uses a single imaging device and the instant invention uses two. The claims do not recite that the imaging devices are different.

Claims 1-7, 10, 13, 16, 19-23, 25, 28 and 31 lack an inventive step under PCT Article 33(3) as being obvious over BEUG et al.
This reference describes the use of histochemical staining with anti-TGFbeta antibodies and the determination of mRNA level using in situ hybridization in tumor cells.
The only difference between the reference and the instant invention is that the reference did not show use the assays.
In view of the suggestion in the reference, it would have been obvious to one of ordinary skill in the art at the time of applicant's invention to use the suggested assays to determine the production of TGFbeta1 in tumor cells.

Applicant argues that the imaging is done on different sections. Again, applicant is arguing limitations not in the claims.

Claims 1-5, 7, 11, 13, 19-23, 25 and 31 lack novelty under PCT Article 33(2) as being anticipated by HENNING et al.
This reference describes the use of cytochemical and histochemical staining to determine molecular markers for tumors in uterine cervical smears. The assays were detected using chromogenic or fluorescent detection. The examples describes the use of an antibody and DNA probe or the use of two antibodies.

Applicant argues that the reference uses a single imaging device to simultaneously view the sample and the instant invention

Supplemental Box

uses two. The claims do not recite that the imaging devices are different. Furthermore, the claims also read on simultaneous detection.

Claims 1-71 meet the criteria set out in PCT Article 33(4), and thus the industrial applicability because the subject matter claimed can be made or used in industry.

Claims 6, 9, 14-15, 17-18, 24, 26, 27, 29, 30 and 32-71 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest the claimed invention.

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WHAT IS CLAIMED IS:

1. A method of identifying cancerous cells in a biological sample comprising:

(a) staining nucleated cells of the biological sample with at least two stains to thereby obtain stained nucleated cells, and;

(b) sequentially and/or simultaneously exposing said stained nucleated cells to at least two imaging modes, to thereby identify the cancerous cells in the biological sample.

2. The method of claim 1, wherein each imaging mode of said at least two imaging modes is specific to a stain of said at least two stains.

3. The method of claim 1, wherein the cancerous cells are associated with a cancer selected from the group consisting of leukemia, lymphoma, brain cancer, cerebrospinal cancer, bladder cancer, prostate cancer, breast cancer, cervix cancer, uterus cancer, ovarian cancer, kidney cancer, esophagus cancer, lung cancer, colon cancer, pancreatic cancer, and melanoma.

4. The method of claim 1, wherein the biological sample is selected from the group consisting of bone marrow cells, lymph nodes cells, peripheral blood, cerebrospinal fluid, urine, effusions, fine needle aspirates, peripheral blood scrapings, paraffin embedded tissues, and frozen sections.

5. The method of claim 1, wherein each stain of said at least two stains is independently selected from the group consisting of a morphological stain, an immunological stain, an activity stain, a cytogenetical stain, *in situ* hybridization stain and a DNA stain.

6. The method of claim 5, wherein said morphological stain is selected from the group consisting of May-Grünwald-Giemsa stain, Giemsa stain, Papanicolau stain, Hematoxylin-Eosin stain and DAPI stain.

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7. The method of claim 5, wherein said immunological stain is selected from the group consisting of fluorescently labeled immunohistochemistry, radiolabeled immunohistochemistry and immunocytochemistry.

8. The method of claim 5, wherein said activity stain is selected from the group consisting of cytochemical stain and substrate binding assay stain.

9. The method of claim 5, wherein said cytogenetical stain is selected from the group consisting of G-banding stain, R-banding stain, Q-banding stain, and C-banding stain.

10. The method of claim 5, wherein said *in situ* hybridization stain is selected from the group consisting of fluorescent *in situ* hybridization (FISH) stain, radiolabeled *in situ* hybridization stain, Digoxigenin labeled *in situ* hybridization stain and biotinylated *in situ* hybridization stain.

11. The method of claim 5, wherein said DNA stain is a DNA-binding fluorescent dye.

12. The method of claim 1, wherein a first stain of said at least two stains is a morphological stain and a second stain of said at least two stains is selected from the group consisting of an immunological stain, an activity stain, an *in situ* hybridization stain, and a DNA stain.

13. The method of claim 1, wherein a first stain of said at least two stains is an immunological stain and a second stain of said at least two stains is selected from the group consisting of a morphological stain, an activity stain, an *in situ* hybridization stain, and a DNA stain.

14. The method of claim 1, wherein a first stain of said at least two stains is an activity stain and a second stain of said at least two stains is selected from the group

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consisting of a morphological stain, an immunological stain, an *in situ* hybridization stain, and a DNA stain.

15. The method of claim 1, wherein a first stain of said at least two stains is a cytogenetical stain and a second stain of said at least two stains is selected from the group consisting of an immunological stain, an *in situ* hybridization stain, and a DNA stain.

16. The method of claim 1, wherein a first stain of said at least two stains is an *in situ* hybridization stain and a second stain of said at least two stains is a DNA stain.

17. The method of claim 1, wherein a first stain of said at least two stains is a DNA stain and a second stain of said at least two stains is an *in situ* hybridization stain.

18. The method of claim 1, wherein step (b) is effected using an automated cell imaging device capable of at least dual imaging.

19. A method of diagnosing cancer in a subject, the method comprising:

(a) obtaining a biological sample from the subject;

(b) staining nucleated cells of said biological sample with at least two stains to thereby obtain stained nucleated cells, and;

(c) sequentially and/or simultaneously exposing said stained nucleated cells to at least two imaging modes, to thereby determine the presence or absence of cancerous cells within said stained nucleated cells, wherein presence of said cancerous cells is indicative of a positive cancer diagnosis.

20. The method of claim 19, wherein each imaging mode of said at least two imaging modes is specific to a stain of said at least two stains.

21. The method of claim 19, wherein the cancer is selected from the group consisting of leukemia, lymphoma, brain cancer, cerebrospinal cancer, bladder cancer, prostate

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cancer, breast cancer, cervix cancer, uterus cancer, ovarian cancer, kidney cancer, esophagus cancer, lung cancer, colon cancer, pancreatic cancer, and melanoma.

22. The method of claim 19, wherein said biological sample is selected from the group consisting of bone marrow cells, lymph nodes cells, peripheral blood, cerebrospinal fluid, urine, effusions, fine needle aspirates and/or peripheral blood scrapings, paraffin embedded tissues, and frozen sections.

23. The method of claim 19, wherein each stain of said at least two stains is independently selected from the group consisting of a morphological stain, an immunological stain, an activity stain, a cytogenetical stain, *in situ* hybridization stain and a DNA stain.

24. The method of claim 23, wherein said morphological stain is selected from the group consisting of May-Grünwald-Giemsa stain, Giemsa stain, Papanicolau stain, Hematoxylin-Eosin stain and DAPI stain.

25. The method of claim 23, wherein said immunological stain is selected from the group consisting of fluorescently labeled immunohistochemistry, radiolabeled immunohistochemistry and immunocytochemistry.

26. The method of claim 23, wherein said activity stain is selected from the group consisting of cytochemical stain and substrate binding assay stain.

27. The method of claim 23, wherein said cytogenetical stain is selected from the group consisting of G-banding stain, R-banding stain, Q-banding stain, and C-banding stain.

28. The method of claim 23, wherein said *in situ* hybridization stain is selected from the group consisting of fluorescent *in situ* hybridization (FISH) stain, radiolabeled *in situ*

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hybridization stain, Digoxigenin labeled *in situ* hybridization stain and biotinylated *in situ* hybridization stain.

29. The method of claim 23, wherein said DNA stain is a DNA-binding fluorescent dye.

30. The method of claim 19, wherein a first stain of said at least two stains is a morphological stain and a second stain of said at least two stains is selected from the group consisting of an immunological stain, an activity stain, an *in situ* hybridization stain, and a DNA stain.

31. The method of claim 19, wherein a first stain of said at least two stains is an immunological stain and a second stain of said at least two stains is selected from the group consisting of a morphological stain, an activity stain, an *in situ* hybridization stain, and a DNA stain.

32. The method of claim 19, wherein a first stain of said at least two stains is an activity stain and a second stain of said at least two stains is selected from the group consisting of a morphological stain, an immunological stain, an *in situ* hybridization stain, and a DNA stain.

33. The method of claim 19, wherein a first stain of said at least two stains is a cytogenetical stain and a second stain of said at least two stains is selected from the group consisting of an immunological stain, an *in situ* hybridization stain, and a DNA stain.

34. The method of claim 19, wherein a first stain of said at least two stains is an *in situ* hybridization stain and a second stain of said at least two stains is a DNA stain.

35. The method of claim 19, wherein a first stain of said at least two stains is a DNA stain and a second stain of said at least two stains is an *in situ* hybridization stain.

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36. The method of claim 19, wherein step (b) is effected using an automated cell imaging device capable of at least dual imaging.

37. A method of identifying transitional cell carcinoma cells in a urine sample comprising:

(a) staining nucleated cells of the urine sample with at least two stains to thereby obtain stained nucleated cells, and;

(b) sequentially and/or simultaneously exposing said stained nucleated cells to at least two imaging modes, to thereby identify the transitional cell carcinoma cells in the urine sample.

38. The method of claim 37, wherein each imaging mode of said at least two imaging modes is specific to a stain of said at least two stains.

39. The method of claim 37, wherein the transitional cell carcinoma cells are associated with bladder cancer and/or kidney cancer.

40. The method of claim 37, wherein the urine sample is obtained via voided urine or catheterization.

41. The method of claim 37, wherein each stain of said at least two stains is independently selected from the group consisting of a morphological stain, an immunological stain, an activity stain, a cytogenetical stain, *in situ* hybridization stain and a DNA stain.

42. The method of claim 41, wherein said morphological stain is selected from the group consisting of May-Grünwald-Giemsa stain, Giemsa stain, Papanicolau stain, Hematoxylin-Eosin stain and DAPI stain.

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43. The method of claim 41, wherein said immunological stain is selected from the group consisting of fluorescently labeled immunohistochemistry, radiolabeled immunohistochemistry and immunocytochemistry.

44. The method of claim 41, wherein said activity stain is selected from the group consisting of cytochemical stain and substrate binding assay stain.

45. The method of claim 41, wherein said cytogenetical stain is selected from the group consisting of G-banding stain, R-banding stain, Q-banding stain, and C-banding stain.

46. The method of claim 41, wherein said *in situ* hybridization stain is selected from the group consisting of fluorescent *in situ* hybridization (FISH) stain, radiolabeled *in situ* hybridization stain, Digoxigenin labeled *in situ* hybridization stain and biotinylated *in situ* hybridization stain.

47. The method of claim 41, wherein said DNA stain is a DNA-binding fluorescent dye.

48. The method of claim 37, wherein a first stain of said at least two stains is a morphological stain and a second stain of said at least two stains is selected from the group consisting of an immunological stain, an activity stain, an *in situ* hybridization stain, and a DNA stain.

49. The method of claim 37, wherein a first stain of said at least two stains is an immunological stain and a second stain of said at least two stains is selected from the group consisting of a morphological stain, an activity stain, an *in situ* hybridization stain, and a DNA stain.

50. The method of claim 37, wherein a first stain of said at least two stains is an activity stain and a second stain of said at least two stains is selected from the group

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consisting of a morphological stain, an immunological stain, an *in situ* hybridization stain, and a DNA stain.

51. The method of claim 37, wherein a first stain of said at least two stains is a cytogenetical stain and a second stain of said at least two stains is selected from the group consisting of an immunological stain, an *in situ* hybridization stain, and a DNA stain.

52. The method of claim 37, wherein a first stain of said at least two stains is an *in situ* hybridization stain and a second stain of said at least two stains is a DNA stain.

53. The method of claim 37, wherein a first stain of said at least two stains is a DNA stain and a second stain of said at least two stains is an *in situ* hybridization stain.

54. The method of claim 37, wherein step (b) is effected using an automated cell imaging device capable of at least dual imaging.

55. A method of diagnosing bladder cancer in a subject, the method comprising:

(a) obtaining a urine sample from the subject;

(b) staining nucleated cells of said urine sample with at least two stains to thereby obtain stained nucleated cells, and;

(c) sequentially and/or simultaneously exposing said stained nucleated cells to at least two imaging modes, to thereby determine the presence or absence of cancerous cells within said stained nucleated cells, wherein presence of said cancerous cells is indicative of a positive cancer diagnosis.

56. The method of claim 55, wherein each imaging mode of said at least two imaging modes is specific to a stain of said at least two stains.

57. The method of claim 55, wherein the urine sample is obtained via voided urine or catheterization.

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58. The method of claim 55, wherein each stain of said at least two stains is independently selected from the group consisting of a morphological stain, an immunological stain, an activity stain, a cytogenetical stain, *in situ* hybridization stain and a DNA stain.

59. The method of claim 58, wherein said morphological stain is selected from the group consisting of May-Grünwald-Giemsa stain, Giemsa stain, Papanicolau stain, Hematoxylin-Eosin stain and/or DAPI stain.

60. The method of claim 58, wherein said immunological stain is selected from the group consisting of fluorescently labeled immunohistochemistry, radiolabeled immunohistochemistry and immunocytochemistry.

61. The method of claim 58, wherein said activity stain is selected from the group consisting of cytochemical stain and substrate binding assay stain.

62. The method of claim 58, wherein said cytogenetical stain is selected from the group consisting of G-banding stain, R-banding stain, Q-banding stain, and C-banding stain.

63. The method of claim 58, wherein said *in situ* hybridization stain is selected from the group consisting of fluorescent *in situ* hybridization (FISH) stain, radiolabeled *in situ* hybridization stain, Digoxigenin labeled *in situ* hybridization stain and biotinylated *in situ* hybridization stain.

64. The method of claim 58, wherein said DNA stain is a DNA-binding fluorescent dye.

65. The method of claim 55, wherein a first stain of said at least two stains is a morphological stain and a second stain of said at least two stains is selected from the

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group consisting of an immunological stain, an activity stain, an *in situ* hybridization stain, and a DNA stain.

66. The method of claim 55, wherein a first stain of said at least two stains is an immunological stain and a second stain of said at least two stains is selected from the group consisting of a morphological stain, an activity stain, an *in situ* hybridization stain, and a DNA stain.

67. The method of claim 55, wherein a first stain of said at least two stains is an activity stain and a second stain of said at least two stains is selected from the group consisting of a morphological stain, an immunological stain, an *in situ* hybridization stain, and a DNA stain.

68. The method of claim 55, wherein a first stain of said at least two stains is a cytogenetical stain and a second stain of said at least two stains is selected from the group consisting of an immunological stain, an *in situ* hybridization stain, and a DNA stain.

69. The method of claim 55, wherein a first stain of said at least two stains is an *in situ* hybridization stain and a second stain of said at least two stains is a DNA stain.

70. The method of claim 55, wherein a first stain of said at least two stains is a DNA stain and a second stain of said at least two stains is an *in situ* hybridization stain.

71. The method of claim 55, wherein step (b) is effected using an automated cell imaging device capable of at least dual imaging.

72. A method of identifying cancerous cells in a biological sample comprising:

(a) staining nucleated cells of the biological sample with a first stain to thereby obtain stained nucleated cells;

(b) exposing said stained nucleated cells to one imaging mode;

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(c) staining said stained nucleated cells with a second stain to thereby obtain stained nucleated cells with a second stain; and

(d) exposing said stained nucleated cells with said second stain to a second imaging mode to thereby identify the cancerous cells in the biological sample.

73. The method of claim 72, further comprising a step of de-staining following said staining with said first stain to thereby remove residual dye of said first stain.

74. A method of identifying cancerous cells in a biological sample comprising:

(a) staining nucleated cells of the biological sample with at least two stains, wherein at least one of said at least two stains is a morphological stain, to thereby obtain stained nucleated cells; and

(b) sequentially and/or simultaneously exposing said stained nucleated cells to at least two imaging modes, to thereby identify the cancerous cells in the biological sample.

75. The method of claim 74, wherein said morphological stain is selected from the group consisting of May-Grünwald-Giemsa stain, Giemsa stain, Papanicolau stain, Hematoxylin-Eosin stain and DAPI stain.